UNITED STATES ARMY ENVIRONMENTAL HYGIENE AGENCY

ABERDEEN PROVING GROUND, MD 21010-5422

PHASE 5
HEALTH HAZARD EVALUATION OF LIQUID MONOPROPELLANTS
STUDY NO. 75-51-0132-85
COMPARATIVE INHALATION TOXICITIES OF LGP 1776, LGP 1845, and HAN
JUNE 1985

DEPARTMENT OF THE ARMY
U. S. ARMY ENVIRONMENTAL HYGIENE AGENCY
ABERDEEN PROVING GROUND, MARYLAND 21010-5422

REPLY TO ATTENTION OF

HSHB-OT

4 L: 1985

SUBJECT: Phase 5, Health Hazard Evaluation of Liquid Monopropellants, Study No. 75-51-0132-85, Comparative Inhalation Toxicities of LGP 1776, LGP 1845, and HAN, June 1985

Commander
US Army Materiel Command
ATTN: AMCSG
5001 Eisenhower Avenue
Alexandria, VA 22333-0001

EXECUTIVE SUMMARY

The purpose, essential findings and conclusions of the enclosed report follows:

a. Purpose. The purpose of this study phase was to determine the comparative acute and subchronic inhalation toxicities of two liquid gun propellant (LGP) formulations designated LGP 1776 and LGP 1845. Hydroxylammonium nitrate (HAN), the major chemical component of each, was also evaluated. Tests in animals were performed to establish a data base from which human hazard projections could be made.

b. Essential Findings. Rats exposed to vapors of the subject compounds for 4 hours were unaffected. Aerosolized LGP 1776 caused toxic signs and one death after a single acute exposure at 2612 mg/m^3. Under the same conditions, LGP 1845 was lethal to 1 out of 20 and 5 out of 20 animals at 1350 and 1603 mg/m^3, respectively. Following 5 or 10 daily airborne exposures in rats to the three chemical formulations, comparable dose-dependent effects were observed. These included hematological, organ-to-body weight ratio and pathological changes.

c. Conclusions. Within the limits of the study, it may be concluded that:

(1) Inhalation of LGP or HAN vapors should not be hazardous to man following an acute low level exposure.

(2) Aerosolized LGP 1845 is comparatively more toxic than LGP 1776 following acute inhalation exposures.

(3) The effects of repeated, sublethal exposures to LGP's 1776 and 1845 are quantitatively similar to those observed with HAN, the major chemical component.

(4) Heinz body formation in red blood cells may be a valid index for monitoring systemic toxicity to HAN-based monopropellants.

FOR THE COMMANDER:

N. JOE THOMPSON
Colonel, MC
Director, Occupational and Environmental Health

CF:
HQDA(DASG-PSP) (wo/encl)
Cdr, ARRADCEN [AMSMC-MP-(A)] (w/encl)
Cdr, HSC (HSCL-P) (w/encl)
Comdt, AHS (HSHA-IPM) (w/encl)
Cdr, AMCCOM [AMSMC-SG(R)] (w/encl)
Cdr, BRL (DRDAR-BLP) (w/encl)
Cdr, WRAMC, (PVNTMED Svc) (w/encl)
Cdr, MEDDAC, Ft Meade (PVNTMED Svc) (2 cy) (w/encl)
Cdr, USAEHA Fld Spt Actv, Ft Meade (w/encl)

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HAN	LGP 1845
Hematology	Monopropellants
Hydroxylammonium nitrate	Rat
Inhalation	Vapor

20. ABSTRACT (Continue on reverse side if necessary and identify by block number)

A comparison of the inhalation toxicities of two liquid gun propellant (LGP) formulations, LGPs 1776 and 1845, was made using rats. Also assessed was the major chemical component of each, hydroxylammonium nitrate (HAN). Rats exposed to saturated vapors of the two LGPs for 8 hours were uneffected. Following single acute aerosol exposures, LGP 1845 was more toxic, with deaths occurring at concentrations of 1350 to 1603 mg/m^3. After 5 or 10 daily aerosol exposures to the three formulations, comparable dose-dependent effects were noted. These included hematological, organ-to-body weight ratio, and

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20. pathological changes, generally at the highest exposure level of 600 mg/m^3. It is concluded that acute exposures to LGP vapors should not be hazardous to man. Also inferred is that the effects of repeated, sublethal exposures to LGPs 1776 and 1845 are quantitatively similar to those observed with HAN, the major chemical component.

DEPARTMENT OF THE ARMY
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REPLY TO
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PHASE 5
HEALTH HAZARD EVALUATION OF LIQUID MONOPROPELLANTS
STUDY NO. 75-51-0132-85
COMPARATIVE INHALATION TOXICITIES OF LGP 1776, LGP 1845, and HAN
JUNE 1985

1. AUTHORITY. Letter, US Army Ballistics Research Laboratory, DRDAR-BLP, 21 August 1978, subject: Request for Toxicity Tests on a Liquid Monopropellant, with indorsement thereto.

2. REFERENCES.

a. See Appendix A for a listing of references.

b. See Appendix B for a statement of quality assurance.

c. See Appendices C thru T for tabular results.

3. PURPOSE. The purpose of this study phase was to determine the acute and subchronic inhalation toxicities of two candidate liquid gun propellants (LGP's) designated LGP 1776 and LGP 1845. Also evaluated was the major chemical component of each, hydroxylammonium nitrate (HAN). The information will provide a data base from which potential health hazards associated with the production, handling, and storage of the subject materials may be determined.

4. BACKGROUND. Several LGP formulations are being considered by the US Army as replacements for conventional munitions. Generally, they contain aqueous mixtures of ammonium nitrates. Earlier toxicity tests in animals have shown that the chemicals are moderately toxic by the oral and dermal routes (Appendix A, reference 1). A chemically-induced hemolytic anemia usually results systemically. Since the potential exists for the accidental aerosolization of the chemicals, the short-term inhalation toxicities of LGP 1776, LGP 1845, and HAN were addressed.

5. TEST MATERIALS. The test materials used in the study were provided by the US Army Ballistic Research Laboratory (USABRL), Aberdeen Proving Ground, Maryland. They included:

a. LGP 1776. Thiokol Lot No. 206.

60 percent HAN; Batch R149/151
20 percent Trimethyl ammonium nitrate; Thiokol Lot No. 128
20 percent Distilled water

b. LGP 1845. Thiokol Lot No. 212.

60 percent HAN; Batch R149/151
20 percent Triethanol ammonium nitrate; Thiokol Lot No. 190
20 percent Distilled water

c. HAN. Indian Head Batch 149/151.

13.2 M HAN

6. ANIMALS.*† Male and female Sprague-Dawley rats were used exclusively. They were obtained from Charles River Breeding Laboratories, Inc., Wilmington, Massachusetts. Animals were maintained on a commercial laboratory diet and water ad libitum. Exposed and control rats were deprived of food during the exposure periods. Ambient conditions were 24° C + 2° C and 45-55 percent relative humidity with a 12-hour, light-dark sequence.

7. METHODS.

a. Acute Inhalation - Saturated Vapor. Acute inhalation studies were conducted by exposing groups of rats to vapors of LGP 1776 and LGP 1845 for a single 8-hour period. Vapors were generated by bubbling dried air through a vessel containing the subject chemical held at room or 50° C temperatures. Groups of six male rats were exposed in a 9-liter glass chamber to room air or to vapors of the test materials drawn from the bubblers. Chamber air flow was 2 L/min and nominal concentrations were calculated from the weight of the material lost from the bubbler through 8 hours. Animals were observed for the development of clinical signs daily and were weighed at 1, 3, 7, and 14 days after exposure. At the end of 14 days, rats were necropsied, organ-to-body weight ratios were calculated, and selected tissues were harvested for histopathological evaluation.

b. Acute Inhalation - LC50. Acute inhalation studies were performed with LGP 1776 and LGP 1845 to determine the median lethal concentration (LC50) of the aerosolized chemicals. A single 4-hour exposure was performed using 10 male and 10 female rats at each dose level. An equal number of animals were tested in atmospheres of ambient room air only. Exposures were performed in a 200-liter glass and stainless steel dynamic flow chamber. Aerosols of the test materials were generated using two

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* In conducting the studies described in this report, the investigators adhered to the "Guide for the Care and Use of Laboratory Animals," US Department of Health, Education, and Welfare Publication No. (NIH) 78-23, revised 1978.

+ The studies reported herein were performed in animal facilities fully accredited by the American Association for the Accreditation of Laboratory Animal Care.

opposed feed generators (18 and 20 ga.) and dried air at 40 psig as the carrier. Chamber air flows were between 12.5 and 20 L/min depending upon the atmosphere desired. Airborne concentrations of LGP's were measured four times during the exposure period by drawing a known volume of chamber air through distilled water and determining the electrical conductivity using a Myron conductivity meter, Model EP, Myron L Co., 6231 Yarrow Drive, Carlsbad, California. Readings were then compared to a standard curve, earlier established using known dilutions of the test materials. Animals were observed immediately after exposure and daily thereafter for development of clinical signs. Body weight measurements were made at 1, 3, 7, and 14 days after exposure. At the end of 14 days, surviving animals were necropsied and any gross lesions recorded.

c. Subchronic Inhalation - 5-or 10-day Exposures. Rats were exposed to aerosols of LGP 1776, LGP 1845, or HAN , 6 hours a day for 5 and 10 days. Weekends were excluded. Atmospheric concentrations of 600, 300, and 75 mg/m^3 were used for all three materials. An additional level, 1200 mg/m^3, was used with LGP 1845. Groups of 15 male or female rats were used for each dose level and compound. Five from each group were removed from the test after the first week, the remaining 10 continuing through 2 weeks (10 exposures). Control animals inhaled only room air. A 200-liter glass and stainless steel dynamic flow chamber was used in all tests. The test materials were aerosolized using two opposed feed generators (18 and 20 ga.) and dried air at 50 psig as the carrier. Chamber air flows were varied between 20 and 50 L/min depending upon the airborne concentrations desired. Chamber atmospheres were measured as described in paragraph 7b. Animals were observed daily for clinical signs and weighed on exposure days 1, 2, 5, 6, and 10. At the end of the 5 or 10-day tests, animals were necropsied and tissues were harvested for histopathological evaluation. Organ-to-body weight ratios were determined. Terminal blood specimens were also collected and complete blood counts (CBC's) and Heinz body determinations performed.

d. Hematology. Heinz body content of erythrocytes was determined morphologically using standard methods (Appendix A, reference 6). Complete blood counts were performed using the Coulter®, Model ZBI6, automated blood counting system. The following parameters were measured:

Total erythrocyte count (RBC)
Hematocrit (Hct)
Hemoglobin (Hgb)
Mean Corpuscular Volume (MCV)

Total leukocyte counts were not performed in rats because counts were artificially elevated due to the presence of debris. This occurs from the destruction of erythrocytes containing Heinz bodies.

® Coulter is a registered trade name of Coulter Electronics, Hialeah, Florida.

8. RESULTS.

a. LGP 1776 - Saturated Vapor. Animals exposed for 8 hours to a saturated vapor of LGP 1776 at ambient or 50° C temperatures were unaffected by the treatment. No toxic signs were observed in any of the rats during the test or the 14-day postexposure period. Normal weight gains were recorded for each group and did not vary significantly from controls. At necropsy, no gross lesions were observed nor were any histological changes seen in tissues. Organ-to-body weight ratios were comparable with controls.

b. LGP 1845 - Saturated Vapor. No adverse effects were noted in rats exposed for 8 hours to a saturated vapor of LGP 1845 heated to 50° C or at room temperature. Test animal weight gains were comparable with controls during the 14-day postexposure period. No gross nor histopathological changes were observed in rat tissues. Organ-to-body weight ratio differences were unremarkable.

c. LGP 1776 - LC50. Male and female rats exposed to airborne concentrations at 2616 mg/m^3 were effected after a single 4-hour aerosol exposure. A blood-tinged exudate was noted around the eyes and nose of all exposed animals. Twenty-four hours after exposure, about one-third of the animals were experiencing severe respiratory distress, i.e., dyspnea, gasping, and wheezing. One of the female rats died. By 48 hours, all signs had abated. At necropsy, 14 days after exposure, no remarkable gross lesions were observed. At the next lower airborne concentration, 1672 mg/m^3, a slight eye and nasal discharge (red-watery) was noted in all male and female test rats immediately after a 4-hour exposure. No signs were observed thereafter nor were any gross lesions noted at necropsy. A tabular presentation of results appears as Appendix C. The acute aerosol LC50 for LGP 1776 in rats was greater than 2616 mg/m^3.

d. LGP 1845 - LC50. Male and female rats exposed to airborne concentrations at 1603 mg/m^3 for 4 hours showed signs of respiratory distress immediately following the exposure. Deaths occurred in 2 of 10 males and 3 of 10 females within 24 hours. Toxic signs had completely cleared by 48 hours postexposure. At necropsy, no lesions were observed grossly. Another 4-hour exposure to male and female rats at 1350 mg/m^3 resulted in the death of one animal (1/20). No other signs were noted in any of the test animals throughout the 14-day postexposure period nor were any gross pathological changes seen at necropsy. A tabular summary of results appears as Appendix D. The acute aerosol LC50 for LGP 1845 in rats was greater than 1603 mg/m^3.

e. Subchronic Inhalation - Airborne Concentrations. The chamber concentrations for LGP 1776, LGP 1845, and HAN were measured analytically as described in paragraph 7b. The Table is a list of the weekly averages of 6-hour, time-weighted averages (TWA) for each material.

TABLE. ACTUAL AIRBORNE CONCENTRATIONS OF LGP 1776, LGP 1845, AND HAN

Mean of Daily Time Weighted Averages

Compound	Study Length (Days)	Target Concentration (mg/m^3) 1200	600	300	75
LGP 1776	5	NA	504	367	88
	10	NA	567	331	89
LGP 1845	5	1216	650	281	81
	10	1204	619	275	75
HAN	5	NA	591	298	101
	10	NA	624	302	99

f. Subchronic Inhalation - LGP 1776.

(1) 5-Day Exposure. Male and female rats exposed to LGP 1776 showed weight gain decrements by the second day of aerosol treatment at the high dose level (600 mg/m^3) which continued through day 5 (Appendix E). This was statistically significant, however, only in females. At necropsy, following the fifth day of exposure, both male and female rats exposed at 300 and 600 mg/m^3 had enlarged spleens. The spleen-to-body weight ratios were also elevated (Appendix F). Liver-to-body weight ratios were depressed in both sexes at the two high dose levels. The RBC and Hct levels in terminal blood specimens from female rats at the high exposure dose were lower than controls (Appendix G). Heinz body formation in erythrocytes was seen in male and female rats at the two highest dose levels. Tissue specimens evaluated from exposed animals showed splenic and hepatic hematopoiesis, but the lesions were not considered compound-related. Inflammatory-type lesions were also noted but could not be judged compound-related because they occurred in comparable incidence and degree among test and control rats.

(2) 10-Day Exposure. Rats exposed to aerosolized LGP 1776 for 10 days showed weight gain decrements by day 2 of treatment at the high dose (600 mg/m^3) (Appendix E). This was noted in both sexes and persisted

throughout the 10-day exposure. Weight gain effects were seen at the middle dose only at day 5 in males and day 10 in females. At necropsy, following the tenth day of exposure, blood specimens showed the presence of Heinz bodies in RBC's in male and female rats at the two high doses (Appendix H). Depressed erythrocyte and MCV counts were also noted in both species at the same inhaled doses, 300 and 600 mg/m^3. An increase in the spleen-to-body weight ratio appeared to be dose-dependent in rats of either sex following 10 exposures to LGP 1776 (Appendix I). Liver-to-body weight ratios were lower than comparable controls in both males and females at the two lower exposure levels. Morphological evaluation of tissue specimens showed splenic hematopoiesis occurring in all spleens examined. The increased severity of splenic hematopoiesis in both sexes in the two high dose groups demonstrated a dose response. Inflammatory lesions commonly seen in laboratory rats were felt to be spontaneous in nature.

g. Subchronic Inhalation - LGP 1845.

(1) 5-Day Exposure. Male and female rats exposed to airborne LGP 1845 at the two high levels, 1200 and 600 mg/m^3, became lethargic and had nasal and eye discharges following the first exposure. After the fifth day of treatment, effects included dyspnea, restlessness, and a blood-tinged exudate. Weight gain decrements began at day 2 and continued through day 5 in both sexes at the highest dose level only (Appendix J). At necropsy, following the fifth exposure, spleens appeared enlarged in rats from the 1200 and 600 mg/m^3 groups. Abnormal organ-to-body weight ratios were observed for spleens (increase) and livers (decrease) of all treated rats except at the lowest dose level (75 mg/m^3) (Appendix K). Heinz body formation was also present in the blood (erythrocytes) of treated rats except at the low dose (Appendix L). A depression in RBC and Hct counts was consistent in rats at the two high doses and was usually accompanied by a decrease in hemoglobin levels. Splenic hematopoiesis was a common histopathological diagnosis in all treatment groups and controls. Grading the degree did not demonstrate a dose response. Although hematopoietic foci were commonly seen in livers, there was a slight increase over controls in both sexes of the 600 mg/m^3 group. Inflammatory lesions were noted in both sexes but were not considered compound-related.

(2) 10-Day Exposure. Rats exposed for 10 days to aerosolized LGP 1845 at the 1200 and 600 mg/m^3 levels had respiratory effects beginning at day 5 of exposure and lasting through day 10. The signs included dyspnea with occasional wheezing. The effects occurred only in about one-third of the rats of either sex at the two high doses and did not necessarily persist in the same animal. Body weight decrements were observed in all animals at the high doses beginning after the second exposure day (Appendix J). Animals necropsied after the tenth exposure had abnormal organ-to-body weight ratios in most organ systems measured (Appendix M). Spleen ratios were increased in all animals and dose levels except the females at 75 mg/m^3. Liver-to-body weight ratios were always lower than comparable controls. Blood specimens collected at necropsy showed the presence of Heinz bodies in erythrocytes except at the lowest treatment level

(Appendix N). The RBC, Hct, and Hgb levels were generally depressed in animals from the two high dose groups. Splenic hematopoiesis was present in nearly all spleens examined morphologically, both test and control. However, the increased severity of hematopoiesis in the 1200 and 600 mg/m^3 treatment groups was considered compound-related. The increased hepatic hematopoiesis was also considered experimentally induced (also at the two high dose levels). The remaining inflammatory lesions were considered spontaneous and not compound induced.

h. Subchronic Inhalation - HAN.

(1) 5-Day Exposure. In male and female rats exposed to airborne HAN at the high dose (600 mg/m^3), the only clinical sign observed was "grayish" eyes. (This is in contrast to the normal red-pink color in albino rats.) This was noted following the fifth exposure day. High-dose female rats showed a weight gain decrement after 5 days (Appendix O). At necropsy, following five HAN exposures, spleen-to-body weight ratios were elevated in male rats at the two high dose levels while the liver ratios were decreased (Appendix P). Female spleen and liver-to-body weight ratios were effected only at the high dose (600 mg/m^3). Blood changes occurred in male and female rats at the high dose level (Appendix Q). The RBC and Hct levels were lower than comparable controls. Heinz body formation was observed in erythrocytes of the treated rats, both sexes, at the high dose (the only level tested). Evaluation of tissue specimens from rats treated for 5 days to aerosolized HAN, indicated a comparable incidence of lesions among control and test animals. On grading the splenic hematopoiesis, there appeared to be an increase in severity in both sexes at the 300 mg/m^3 level which was considered compound-related. The remaining inflammatory lesions were not equated with treatment.

(2) 10-Day Exposure. Nearly all of the effects observed following exposure to airborne HAN occurred at the high exposure level (600 mg/m^3). These included "grayish" eyes seen in male and female rats beyond day 4 of exposure and sneezing which occurred immediately after each day's exposure beginning at day 6. The same rats (high dose) showed weight gain decrements from day 5 (Appendix O). At necropsy, organ-to-body weight ratios of spleens were increased at both high doses and liver ratios were decreased (Appendix R). In female rats, kidney ratios were elevated except at the low dose which remained unchanged. The RBC, Hct, and Hgb levels in blood from high dose male and female rats were depressed after 10 HAN exposures (Appendix S). Erythrocytes from high dose rats contained Heinz bodies (the only dose level measured). Histopathological changes were seen in tissues from both treatment and control animals. The degree of severity of splenic hematopoiesis increased in the two high treatment groups which was considered related to the administration of the test chemical. A mild increase in hepatic hematopoiesis in high dose females was also considered related to treatment. Commonly seen inflammatory lesions were not considered compound-related.

9. DISCUSSION.

a. The inhalation of saturated vapors of LGP 1776 and LGP 1845 was without effect in rats. Given the aqueous nature of the test substances, this was not unexpected. Hydroxylammonium nitrate was not included in this test sequence since both of the materials studied represent the end-use products. In man, the short-term hazards associated with the inhalation of LGP 1776 and LGP 1845 vapors should be minimal.

b. Of the two LGP'S tested by acute aerosol inhalation to rats, LGP 1845 appears to be the more toxic following a single 4-hour exposure. At an airborne concentration of 1603 mg/m^3, 25 percent of the test animals died. For LGP 1776, only one death was observed, occurring at 2616 mg/m^3. With both propellants, deaths occurred within 24 hours of exposure, and all toxic signs had abated by 48 hours. No untoward effects were noted through the 14-day observation period or at necropsy. This suggests that the effects of an acute, sublethal inhalation insult do not result in debilitating illness in rats, nor would it be anticipated in man.

c. A comparison of the effects in rats of inhaled LGP 1776, LGP 1845, and HAN aerosols, following 5 or 10 daily exposures, is summarized in Appendix T. Generally, the two liquid propellants and HAN, the major component of each, elicit similar effects in rats at comparable sublethal doses. Nearly all of the changes appear to be dose-dependent. The most consistent effects were Heinz body formation in blood at the two higher dose levels and organ-to-body weight ratio changes which persisted in most cases into the lowest dose level groups. While the increased size and weight of rat spleens was the most remarkable finding at necropsy at the two higher dose levels, a more subtle but significant decrease in the liver-to-body weight ratios was seen throughout the entire dosage range. Unlike the spleen, liver weight ratio changes occurred by the end of the first week of exposures to LGP 1776 and LGP 1845. An earlier, long-term study with HAN (90-day inhalation) showed a similar trend towards reduced liver-to-body weight ratios in male and female rats exposed at 33 mg/m^3 (Appendix A, reference 5). Although the finding in that study was not statistically significant when compared with controls, the trend was consistent. In the same study, Heinz body formation appeared in the blood of HAN-exposed dogs at 300 and 100 mg/m^3 after the first 2 weeks of exposure. Based on the current test data, it would appear that both the dog and rat suffer a comparable blood dyscrasia at nearly identical levels of airborne HAN. This point may become noteworthy in the monitoring for potential systemic toxicity of HAN-based LGP's in man.

10. CONCLUSIONS. The following conclusions are based on the results (paragraph 8) of this study.

a. The vapors arising from the LGP's, LGP 1776 and LGP 1845, should not present an inhalation hazard to man following an acute exposure.

b. Liquid gun propellant 1845 is comparatively more toxic than LGP 1776 by the aerosol inhalation route as demonstrated in male and female rats.

c. Heinz body formation in red blood cells may be a valid index of systemic toxicity in man to HAN-based monopropellants.

d. The effects of repeated, sublethal exposures to LGP's 1776 and 1845 are quantitatively similar to those observed with HAN, the major chemical component.

HUBERT L. SNODGRASS, JR
Biologist
Toxicology Division

Approved:

MAURICE H. WEEKS
Chief, Toxicology Division

APPENDIX A

REFERENCES

1. McCreesh, A. H., L. W. Metker, J. Bergmann and M. H. Weeks, "Hazard Assessment of Liquid Propellant Formulations." In: 1980 JANNAF (Joint Army, Navy, NASA, Air Force) Safety and Environmental Protection Specialist Session, Chemical Propulsion Information Agency Publication 313, The Johns Hopkins University Applied Physics Laboratory, Laurel, Maryland, pp 163-169 (April 1980)

2. Letter, USAEHA, HSE-LT/WP, 21 December 1979, Phase 1, Physiological and Pharmacological Effects Following Oral Administration of Monopropellants, Special Study No. 75-51-0132-80, August 1978 - September 1979.

3. Letter, USAEHA, HSHB-LT/WP, 16 August 1982, subject: Health Hazard Evaluation of Liquid Monopropellants, Special Study No. 75-51-0132-82, Phase 2, Effects of Dermal Administration of Hydroxylammonium Nitrate, May 1980 - March 1982.

4. Letter, USAEHA, HSHB-OT/WP, 25 April 1984, subject: Phase 3, Health Hazard Evaluation of Liquid Monopropellants, Special Study No. 75-51-0132-84, Range Finding Studies on the Effects of Hydroxylammonium Nitrate in Animals, September 1980 - June 1983.

5. Letter, USAEHA, HSHB-OT, subject: Phase 4, Health Hazard Evaluation of Liquid Monopropellants, Special Study No. 75-51-0132-85, Subchronic Inhalation of Hydroxylammonium Nitrate (HAN), January 1985.

6. US Army Environmental Hygiene Agency, Toxicology Division, Standard Operating Procedure (SOP), No. 44, Heinz Body Determinations (March 1980)

7. Title 21, Code of Federal Regulations (CFR), 1985 rev, Part 58, Good Laboratory Practice for Nonclinical Laboratory Studies.

8. Title 40, CFR, 1984 rev, Part 162, Regulations for the Enforcement of the Federal Insecticide, Fungicide, and Rodenticide Act.

APPENDIX B

ANALYTICAL QUALITY ASSURANCE

The Analytical Quality Assurance Office certifies the following with regard to this study:

a. This study was conducted in accordance with:

(1) Standing Operating Procedures developed by the Toxicology Division, USAEHA.

(2) Title 21, Code of Federal Regulations, 1985 rev, Part 58, Good Laboratory Practice for Nonclinical Laboratories Studies.

b. Facilities were inspected during its operational phase to insure compliance with paragraph a above.

c. The information presented in this report accurately reflects the raw data generated during the course of conducting the study.

Paul V. Sneeringer

PAUL V. SNEERINGER, Ph.D.
Chief, Analytical Quality
Assurance Office

APPENDIX C

COMPOUND: LGP 1776

TOXICITY CATEGORY*: USAEHA STUDY NO. 75-51-0132-85

ACUTE AEROSOL LC 50

LC50 >2616 mg/m³ SPECIES Sprague-Dawley Rats

ROUTE Inhalation SEX Male and Female

CONDITIONS Single 4 hour exposure

Sex	Conc	Onset of signs (s), mortality (m)										Mortality Frac.	Initial Body Wt.	Body Wt (g)			
		Hours			Days									Days			
		0-4	4-12	12-24	2	3	4	5	6	7	8-14			1	3	7	14
Male	2616	S10[1,2]		S4[3,4]								0/10	94±9	89 ±9	105 ±9	137 ±12	199 ±18
	Control											0/10	97±6	102 ±7	114 ±8	145 ±11	208 ±16
Female	2616	S10[1,2]		S2[3,4] M1								1/10	91±7	84 ±6	98 ±6	126 ±7	169 ±6
	Control											0/10	94±6	98 ±6	107 ±5	133 ±7	174 ±13
Male	1672	S10[5]										0/10	109±6	105 ±7	122 ±8	155 ±10	211 ±12
	Control											0/10	108±6	113 ±7	126 ±8	159 ±11	217 ±14
Female	1672	S10[5]										0/10	104±4	98 ±6	115 ±5	137 ±4	170 ±10
	Control											0/10	100±4	104 ± 4	112 ±5	137 ±7	168 ±11

S[1]- Ruffled coat; S[2] - Dried red exudate around eyes and nose; S[3] - dyspnea; S[4] - gasping, wheezing; S[5] - minor eye and nasal discharge (red - watery)

Necropsy - No gross lesions were observed 14 days after exposure.

*40 CFR 162

APPENDIX D

COMPOUND: LGP 1845

TOXICITY CATEGORY*: USAEHA STUDY NO. 75-51-0132-85

ACUTE AEROSOL LC 50

LC50 >1603 mg/m³ SPECIES Sprague-Dawley Rats

ROUTE Inhalation SEX Male and Female

CONDITIONS Single 4-hour exposure

Sex	Conc	Onset of signs (s), mortality (m) Hours 0-4	Hours 4-12	Hours 12-24	Days 2	3	4	5	6	7	8-14	Mortality Frac.	Initial Body Wt.	Body Wt (g) Days 1	3	7	14
Male	1603	S1[1,2]		M2								2/10	92±2	87 ±5	100 ±4	141 ±3	205 ±6
	Control											0/10	102±7	107 ±7	124 ±10	154 ±12	214 ±17
Female	1603	S3[1]		M3								3/10	85±3	79 ±5	92 ±4	121 ±5	156 ±6
	Control											0/10	98±6	103 ±6	114 ±5	138 ±8	174 ±13
Male	1350											0/10	120±5	112 ±10	133 ±11	169 ±12	218 ±19
	Control											0/10	113±7	119 ±9	133 ±9	166 ±11	217 ±14
Female	1350			M1								1/10	109±4	105 ±5	120 ±6	143 ±7	176 ±8
	Control											0/10	104±4	108 ±5	119 ±6	139 ±8	168 ±11

S^1 - labored breathing; S^2 - wheezing.

Necropsy - No gross lesions were observed 14-days after exposure.

*40 CFR 162

APPENDIX E

LGP 1776
5- AND 10-DAY AEROSOL EXPOSURE
RAT BODY WEIGHTS

Sex	Exposure Day	Exposure Level: Control	600 mg/m³	300 mg/m³	75 mg/m³
Males	1	142 ± 10	151 ± 2	115 ± 8	110 ± 4
	2	145 ± 10	139 ± 13	114 ± 7	117 ± 4
	5	165 ± 10	149 ± 15	136 ± 9	136 ± 4
Females	1	125 ± 9	123 ± 5	110 ± 4	99 ± 2
	2	129 ± 8	119 ± 5*	109 ± 8	105 ± 3
	5	144 ± 10	127 ± 7*	125 ± 9	122 ± 3
Males	1	139 ± 8	141 ± 8	115 ± 6	107 ± 7
	2	145 ± 7	137 ± 7*	114 ± 4	115 ± 7
	5	167 ± 7	149 ± 9*	136 ± 4*	136 ± 9
	6	189 ± 10	170 ± 8*	161 ± 6	159 ± 12
	10	221 ± 10	191 ± 10*	188 ± 6	192 ± 14
Females	1	123 ± 4	120 ± 6*	109 ± 6	101 ± 4
	2	127 ± 5	118 ± 7*	109 ± 6	107 ± 4
	5	143 ± 7	125 ± 9*	125 ± 8	124 ± 5
	6	158 ± 6	140 ± 9*	146 ± 10	140 ± 8
	10	173 ± 8	152 ± 9*	166 ± 12*	159 ± 10

* Significantly lower ($p>0.05$) than comparable control group.
NOTE: Control group for the 600 mg/m³ exposure level only is presented.

APPENDIX F

LGP 1776
5-DAY AEROSOL EXPOSURE
ORGAN-TO-BODY WEIGHT RATIOS IN MALE AND FEMALE RATS

Level mg/m³		Body Wt gm	Lung	Liver	Kidney	Spleen	Testes
Control,	male	165±10	0.65±0.05	4.47±0.26	0.96±0.05	0.34±0.04	0.94±0.11
	female	144±10	0.75±0.06	4.95±0.42	0.96±0.10	0.34±0.01	
600,	male	149±14	0.75±0.05*	3.99±0.27*	0.96±0.02	0.49±0.12*	1.13±0.09
	female	127±7*	0.77±0.09	3.87±0.28*	0.99±0.04	0.58±0.05*	
Control,	male	148±12	0.68±0.09	4.96±0.44	1.06±0.07	0.39±0.09	0.81±0.20
	female	132±6	0.67±0.03	4.84±0.19	0.98±0.08	0.34±0.07	
300,	male	136±9	0.81±0.10	3.94±0.52*	1.04±0.06	0.54±0.04*	0.98±0.16
	female	125±9	0.79±0.17	4.09±0.30*	1.00±0.07	0.52±0.06*	
Control,	male	144±7	0.69±0.06	4.57±0.28	1.04±0.09	0.35±0.03	0.92±0.06
	female	121±3	0.69±0.03	4.63±0.35	1.07±0.04	0.38±0.08	
75,	male	134±4*	0.68±0.03	3.73±0.15*	1.02±0.07	0.37±0.07	0.98±0.11
	female	122±3	0.71±0.04	3.95±0.33*	1.03±0.05	0.41±0.06	

* Significantly different from controls ($p<0.05$).

APPENDIX G

LGP 1776
5-DAY AEROSOL EXPOSURE
RAT HEMATOLOGICAL MEASUREMENTS

Level (mg/m^3)	RBC ($10^6/\mu L$)	MCV (μ^3)	Hct (%)	Hgb (g/dL)	Heinz Bodies
Control, male	4.7±0.5	63±0	30±3	11.8±1.4	NEG
female	5.3±0.4	63±2	33±2	12.9±0.6	NEG
600, male	4.5±0.4	65±4	29±2	12.4±0.5	POS
female	4.4±0.4*	64±2	28±2*	12.2±0.8	POS
Control, male	4.6±0.5	66±2	31±3	10.8±0.7	NEG
female	4.9±0.5	65±3	32±2	11.4±0.8	NEG
300, male	4.5±0.3	66±2	30±2	11.0±0.5	POS
female	4.7±0.2	65±1	31±1	11.4±0.3	POS
Control, male	4.7±0.4	67±3	31±1	11.3±0.5	NEG
female	4.4±0.4	69±5	30±1	11.1±0.6	NEG
75, male	4.9±0.2	65±1	32±1	11.6±0.5	NEG
female	5.0±0.6	65±4	32±2	11.8±0.5	NEG

* Significantly different from controls ($p<0.05$).

APPENDIX H

LGP 1776
10-DAY AEROSOL EXPOSURE
RAT HEMATOLOGICAL MEASUREMENTS

Level (mg/m^3)	RBC ($10^6/\mu L$)	MCV (μ^3)	Hct (%)	Hgb (g/dL)	Heinz Bodies
Control, male	5.2±0.3	64±2	33±1	12.7±0.5	NEG
female	5.8±0.2	61±2	35±2	13.3±0.6	NEG
600, male	4.5±0.3*	78±4*	35±3	12.5±0.8	POS
female	4.6±0.4*	72±4*	33±2*	12.2±0.7*	POS
Control, male	5.1±0.3	63±2	32±2	12.4±1.0	NEG
female	5.6±0.3	63±2	35±1	13.3±0.4	NEG
300, male	4.6±0.3*	72±2*	33±2	12.2±0.9	POS
female	4.8±0.3*	70±3*	34±2	12.8±0.7	POS
Control, male	5.0±0.3	64±1	32±2	12.1±0.8	NEG
female	5.4±0.3	63±2	34±1	6.5±1.2	NEG
75, male	5.3±0.3	63±3	33±1	10.3±2.0	NEG
female	5.3±0.3	63±2	33±2	12.2±0.7	NEG

* Significantly different from controls ($p<0.05$).

APPENDIX I

LGP 1776
5-DAY AEROSOL EXPOSURE
ORGAN-TO-BODY WEIGHT RATIOS IN MALE AND FEMALE RATS

Level mg/m³		Body Wt gm	Lung	Liver	Kidney	Spleen	Testes
Control,	male	221±10	0.61±0.06	5.05±0.38	0.94±0.07	0.30±0.03	1.04±0.14
	female	173±8	0.66±0.07	4.52±0.72	0.91±0.06	0.30±0.04	
600,	male	191±10*	0.58±0.08	3.91±0.43*	0.83±0.07*	0.66±0.08*	1.12±0.13
	female	152±9*	0.72±0.10	3.92±0.19*	0.92±0.04	0.65±0.07*	
Control,	male	184±8	0.67±0.08	4.92±0.16	0.91±0.05	0.33±0.05	0.97±0.06
	female	154±7	0.68±0.04	4.67±0.38	0.96±0.06	0.29±0.05	
300,	male	188±6	0.61±0.06	4.22±0.24*	0.92±0.06	0.56±0.05*	1.01±0.06
	female	166±12*	0.69±0.06	4.51±0.26	0.96±0.07	0.51±0.06*	
Control,	male	192±9	0.72±0.08	4.91±0.30	0.96±0.03	0.34±0.04	0.93±0.10
	female	157±14	0.76±0.08	4.55±0.42	1.04±0.05	0.30±0.04	
75,	male	192±14	0.70±0.06	4.31±0.43*	0.96±0.05	0.34±0.05	1.03±0.08*
	female	159±10	0.83±0.11	4.27±0.27	0.98±0.05*	0.35±0.05	

* Significantly different from controls ($p<0.05$).

APPENDIX J

LGP 1845
5- AND 10-DAY AEROSOL EXPOSURE
RAT BODY WEIGHTS (gm)

Sex	Exposure Day	Exposure Level: Control	1200 mg/m³	600 mg/m³	300 mg/m³	75 mg/m³
Males	1	113 ± 5	112 ± 7	111 ± 7	127 ± 7	84 ± 10
	2	119 ± 4	106 ± 4*	110 ± 10	130 ± 7	89 ± 10
	5	141 ± 8	108 ± 6*	126 ± 17	149 ± 4	112 ± 4
Females	1	115 ± 6	111 ± 7	106 ± 5	112 ± 5	126 ± 5
	2	119 ± 6	105 ± 8*	106 ± 5	113 ± 6	125 ± 4
	5	135 ± 10	110 ± 9*	117 ± 8	129 ± 4	141 ± 6
Males	1	112 ± 6	112 ± 5	107 ± 9	126 ± 7	94 ± 7
	2	117 ± 6	107 ± 4*	107 ± 9*	131 ± 8	100 ± 7
	5	138 ± 8	114 ± 7*	122 ± 10*	150 ± 8	121 ± 7
	6	162 ± 10	137 ± 9*	147 ± 10*	174 ± 8	148 ± 8
	10	189 ± 13	135 ± 14*	165 ± 9*	203 ± 11	181 ± 11
Females	1	110 ± 6	111 ± 5	109 ± 6	112 ± 5	84 ± 9
	2	114 ± 6	105 ± 8*	105 ± 2*	115 ± 5	89 ± 9
	5	131 ± 9	110 ± 11*	116 ± 3*	131 ± 7	107 ± 11
	6	147 ± 11	128 ± 10*	136 ± 3*	147 ± 7	127 ± 11
	10	159 ± 12	128 ± 9*	145 ± 6*	164 ± 9	151 ± 12

* Significantly lower ($p>0.05$) than comparable control group.
NOTE: Represents control group for the 1200 mg/m³ exposure level only.

APPENDIX K

LGP 1845
5-DAY AEROSOL EXPOSURE
ORGAN-TO-BODY WEIGHT RATIOS IN MALE AND FEMALE RATS

Level mg/m³		Body Wt gm	Lung	Liver	Kidney	Spleen	Testes
Control,	male	141±8	0.81±0.06	4.30±0.26	1.02±0.07	0.35±0.07	1.06±0.04
	female	135±10	0.89±0.14	4.35±0.31	1.03±0.08	0.36±0.03	
1200,	male	108±6*	1.02±0.06*	3.92±0.33	1.11±0.13	0.76±0.16*	1.43±0.2*
	female	110±9*	0.98±0.12	3.68±0.17*	1.07±0.05	0.74±0.17*	
Control,	male	131±9	0.79±0.05	4.76±0.10	1.02±0.09	0.36±0.03	0.93±0.05
	female	126±3	0.88±0.06	4.19±0.26	1.00±0.05	0.28±0.04	
600,	male	127±17	0.81±0.04	3.95±0.24*	1.02±0.04	0.68±0.09*	0.97±0.08
	female	117±8	0.87±0.05	3.71±0.29*	1.04±0.10	0.61±0.04*	
Control	male	155±8	0.74±0.10	4.55±0.26	0.97±0.06	0.33±0.01	0.95±0.10
	female	134±5	0.72±0.05	4.50±0.20	1.01±0.04	0.31±0.02	
300,	male	149±4	0.67±0.12	3.86±0.29*	0.96±0.03	0.44±0.05*	1.03±0.08
	female	134±5	0.72±0.05	4.50±0.20	1.01±0.04	0.31±0.02	
Control,	male	111±14	0.80±0.03	4.81±0.32	1.13±0.08	0.44±0.06	0.89±0.11
	female	146±13	0.76±0.10	4.73±0.22	1.08±0.06	0.38±0.08	
75,	male	112±14	0.86±0.07	4.31±0.11*	1.06±0.08	0.45±0.03	0.92±0.08
	female	141±6	0.74±0.11	4.61±0.26	1.01±0.05	0.33±0.03	

* Significantly different from controls ($p<0.05$).

APPENDIX L

LGP 1845
5-DAY AEROSOL EXPOSURE
RAT HEMATOLOGICAL MEASUREMENTS

Level (mg/m^3)	RBC ($10^6/\mu L$)	MCV (μ^3)	Hct (%)	Hgb (g/dL)	Heinz Bodies
Control, male	5.3±0.6	67±1	35±4	12.7±1.3	NEG
female	5.2±0.4	67±3	35±2	13.2±0.9	NEG
1200, male	4.0±0.3*	73±4*	29±1*	12.5±0.9	POS
female	4.4±0.3*	69±2	30±2*	12.7±0.6	POS
Control, male	5.3±0.2	67±1	35±1	12.0±0.2	NEG
female	5.3±0.2	65±2	34±1	13.1±0.5	NEG
600, male	4.3±0.3*	73±4*	31±4*	11.5±0.7*	POS
female	4.4±0.4*	67±3	29±1*	11.6±0.4*	POS
Control, male	4.4±0.3	74±2	33±2	11.0±0.6	NEG
female	4.6±0.3	72±2	34±2	11.1±0.6	NEG
300, male	4.8±0.2	75±3	36±2*	11.9±0.5*	POS
female	4.7±0.2	72±2	34±1	11.2±0.3	POS
Control, male	4.8±0.2	65±2	31±1	11.0±0.4	NEG
female	5.4±0.7	62±3	33±3	12.3±1.3	NEG
75, male	5.2±0.2*	66±3	34±1*	11.5±0.5	NEG
female	6.1±0.3	61±1	36±1	13.2±0.4	NEG

* Significantly different from controls ($p<0.05$).

APPENDIX M

LGP 1845
5-DAY AEROSOL EXPOSURE
ORGAN-TO-BODY WEIGHT RATIOS IN MALE AND FEMALE RATS

Level mg/m^3		Body Wt gm	Lung	Liver	Kidney	Spleen	Testes
Control,	male	189±13	0.70±0.11	4.61±0.31	0.96±0.04	0.32±0.05	1.00±0.08
	female	159±12	0.74±0.15	4.55±0.48	1.02±0.08	0.27±0.03	
1200,	male	135±14*	0.85±0.16*	3.77±0.15	1.10±0.14*	1.46±0.23	1.29±0.14*
	female	128±9*	0.96±0.10*	4.03±0.51*	1.20±0.37	1.57±0.33*	
Control,	male	192±11	1.32±0.10	4.76±0.51	0.93±0.04	0.30±0.04	1.05±0.13
	female	165±8	0.73±0.07	4.89±0.26	0.96±0.05	0.27±0.03	
600,	male	165±9*	1.45±0.45*	4.05±0.27*	0.91±0.07	0.88±0.17*	1.20±0.06*
	female	145±7*	0.79±0.07	4.21±0.30*	0.96±0.07	0.75±0.18*	
Control	male	206±15	0.67±0.10	4.48±0.26	0.89±0.09	0.32±0.05	1.03±0.12
	female	172±10	0.67±0.06	4.71±0.28	0.96±0.10	0.31±0.05	
300,	male	203±11	0.63±0.09	4.16±0.24*	0.85±0.06	0.56±0.06*	1.00±0.05
	female	164±9	0.75±0.07*	4.26±0.24*	0.94±0.06	0.55±0.09*	
Control,	male	180±17	0.64±0.07	4.77±0.33	0.88±0.06	0.32±0.02	0.89±0.06
	female	144±10	0.71±0.17	4.65±0.42	0.91±0.06	0.29±0.05	
75,	male	181±11	0.64±0.07	4.35±0.26*	0.89±0.05	0.36±0.03*	0.97±0.10
	female	151±12	0.71±0.09	4.28±0.16*	0.88±0.04	0.32±0.04	

* Significantly different from controls ($p<0.05$).

APPENDIX N

LGP 1845
10-DAY AEROSOL EXPOSURE
RAT HEMATOLOGICAL MEASUREMENTS

Level (mg/m^3)	RBC ($10^6/\mu L$)	MCV (μ^3)	Hct (%)	Hgb (g/dL)	Heinz Bodies
Control, male	5.4±0.2	64±2	34±1	13.0±0.4	NEG
female	5.6±0.4	66±2	35±3	13.0±0.9	NEG
1200, male	2.9±0.6*	100±6*	28±4*	10.4±2.1*	POS
female	2.9±0.1*	99±5*	28±2*	9.6±0.3*	POS
Control, male	5.2±0.4	73±2	38±2	12.5±0.5	NEG
female	5.2±0.5	73±3	37±3	13.3±1.0	NEG
600, male	3.6±0.7*	90±6*	32±4*	11.8±1.6*	POS
female	3.9±0.4*	85±4*	33±3*	11.3±1.1*	POS
Control, male	5.5±0.3	66±3	35±1	13.0±0.4	NEG
female	5.3±0.3	63±2	33±1	13.1±0.4	NEG
300, male	4.3±0.3*	71±3*	30±2*	11.8±0.6*	POS
female	4.5±0.3*	66±3*	29±2*	11.8±0.6*	POS
Control, male	5.5±0.4	66±2	36±2	12.9±0.6	NEG
female	5.8±0.5	62±2	36±3	12.7±1.0	NEG
75, male	4.6±0.4*	64±3	30±3*	12.2±1.0	NEG
female	5.4±0.4	64±1*	34±3	12.0±1.0	NEG

* Significantly different from controls ($p<0.05$).

APPENDIX O

HAN
5- AND 10-DAY AEROSOL EXPOSURE
RAT BODY WEIGHTS (gm)

Sex	Exposure Day	Exposure Level (mg/m^3) Control	600	300	75
Males	1	105 ± 9	108 ± 12	131 ± 5	93 ± 4
	2	108 ± 10	102 ± 20	132 ± 9	95 ± 5
	5	127 ± 11	108 ± 14	150 ± 11	112 ± 10
Females	1	105 ± 10	104 ± 8	112 ± 7	100 ± 14
	2	109 ± 11	103 ± 10	113 ± 9	104 ± 16
	5	127 ± 11	109 ± 12*	126 ± 14	121 ± 18
Males	1	111 ± 14	110 ± 10	116 ± 9	119 ± 13
	2	114 ± 13	107 ± 13	118 ± 11	125 ± 14
	5	136 ± 17	115 ± 11*	137 ± 12	144 ± 16
	6	159 ± 20	133 ± 13*	159 ± 15	169 ± 18
	10	189 ± 18	124 ± 15*	176 ± 18*	200 ± 21
Females	1	103 ± 9	102 ± 10	112 ± 8	96 ± 13
	2	107 ± 9	95 ± 16	113 ± 4	100 ± 14
	5	123 ± 11	98 ± 18*	131 ± 5	111 ± 17
	6	137 ± 15	114 ± 17*	148 ± 8	128 ± 19
	10	148 ± 13	103 ± 18*	162 ± 9	147 ± 21

* Significantly lower ($p>0.05$) than comparable control group.
NOTE: Only the control group for the 600 mg/m^3 exposure level is presented.

APPENDIX P

HAN
5-DAY AEROSOL EXPOSURE
ORGAN-TO-BODY WEIGHT RATIOS IN MALE AND FEMALE RATS

Level mg/m³		Body Wt gm	Lung	Liver	Kidney	Spleen	Testes
Control,	male	127±11	0.63±0.07	4.35±0.34	1.14±0.09	0.37±0.05	1.15±0.06
	female	127±11	0.74±0.08	4.44±0.40	0.88±0.06	0.34±0.06	
600,	male	108±14	0.84±0.13	3.56±0.28*	0.92±0.04	0.52±0.05*	1.15±0.06
	female	109±12	0.81±0.14	3.50±0.37*	0.92±0.09	0.64±0.14*	
Control	male	153±10	0.71±0.05	4.39±0.19	0.89±0.09	0.38±0.03	1.03±0.10
	female	132±16	0.76±0.08	4.57±0.25	0.98±0.07	0.41±0.07	
300,	male	150±11	0.72±0.03	3.94±0.03*	0.93±0.06	0.49±0.07*	1.13±0.07
	female	126±14	0.83±0.05	4.19±0.49	0.99±0.02	0.54±0.18	
Control,	male	118±6	0.82±0.06	4.38±0.16	1.03±0.06	0.53±0.14	0.89±0.06
	female	125±9	0.81±0.05	4.41±0.22	0.99±0.06	0.42±0.09	
75,	male	112±10	0.86±0.03	4.16±0.31	1.17±0.13	0.56±0.17	0.87±0.06
	female	121±18	0.84±0.07	4.25±0.15	1.05±0.07	0.41±0.10	

* Significantly different from controls ($p<0.05$).

APPENDIX Q

HAN
5-DAY AEROSOL EXPOSURE
RAT HEMATOLOGICAL MEASUREMENTS

Level (mg/m^3)	RBC ($10^6/\mu L$)	MCV (μ^3)	Hct (%)	Hgb (g/dL)	Heinz Bodies
Control, male	5.4±0.4	62±2	33±2	11.6±0.8	NEG
female	5.5±0.3	63±3	34±2	12.4±0.3	NEG
600, male	4.7±0.5	63±3	28±2	11.7±1.0	POS
female	4.7±0.4	64±3	29±2	12.1±0.6	POS
Control, male	5.2±0.3	60±1	32±2	11.6±0.8	---
female	5.0±0.4	61±1	31±3	11.7±1.2	---
300, male	5.4±0.2	62±2	34±1	12.1±0.3	---
female	5.5±0.4	60±3	33±2	12.1±0.3	---
Control, male	4.8±0.7	64±2	31±4	11.5±1.2	---
female	4.9±0.3	62±2	31±2	11.6±0.6	---
75, male	5.1±0.3	62±3	32±2	11.5±0.6	---
female	4.0±0.3	62±2	31±2	11.6±0.5	---

* Significantly different from controls ($p<0.05$).

APPENDIX R

HAN
10-DAY AEROSOL EXPOSURE
ORGAN-TO-BODY WEIGHT RATIOS IN MALE AND FEMALE RATS

Level mg/m^3		Body Wt gm	Lung	Liver	Kidney	Spleen	Testes
Control,	male	189±18	0.66±0.07	4.57±0.27	0.89±0.05	0.35±0.05	1.05±0.09
	female	148±13	0.74±0.07	4.48±0.39	0.86±0.06	0.32±0.03	
600,	male	124±15*	0.82±0.10*	3.49±0.46*	0.99±0.15	1.32±0.29*	1.5±0.25*
	female	103±18	0.91±0.09*	3.54±0.24*	1.04±0.07*	1.11±0.20*	
Control	male	197±15	0.68±0.08	4.67±0.28	0.89±0.03	0.40±0.04	1.01±0.09
	female	164±11	0.75±0.07	4.73±0.26	0.91±0.04	0.38±0.08	
300,	male	176±18*	0.77±0.08*	4.01±0.22*	0.93±0.07	0.66±0.07*	1.00±0.24
	female	162±9	0.71±0.10	4.46±0.15*	0.99±0.08*	0.61±0.08*	
Control,	male	209±15	0.74±0.18	4.94±0.28	0.88±0.05	0.32±0.02	0.89±0.05
	female	148±15	0.79±0.08	4.69±0.24	0.99±0.06	0.44±0.05	
75,	male	200±21	0.79±0.14	4.33±0.25*	0.89±0.03	0.37±0.04	0.91±0.12
	female	147±21	0.80±0.10	4.23±0.60*	0.97±0.10	0.37±0.07	

* Significantly different from controls ($p<0.05$).

APPENDIX S

HAN
10-DAY AEROSOL EXPOSURE
RAT HEMATOLOGICAL MEASUREMENTS

Level (mg/m^3)	RBC ($10^6/\mu L$)	MCV (μ^3)	Hct (%)	Hgb (g/dL)	Heinz Bodies
Control, male	5.8±0.3	60±4	35±1	12.5±0.6	NEG
female	6.0±0.3	60±2	36±1	13.0±0.5	NEG
600, male	3.4±0.5*	89±7*	29±8*	10.1±1.4*	POS
female	3.4±0.4*	84±7*	29±4*	10.0±0.8*	POS
Control, male	5.9±0.2	61±1	36±1	12.8±0.6	---
female	5.9±0.4	59±1	35±2	13.0±0.5	---
300, male	5.5±0.2*	66±4*	36±2	12.7±0.3	---
female	5.6±0.3*	66±3*	37±2	12.7±0.6	---
Control, male	5.5±0.4	62±1	34±2	12.7±0.7	---
female	5.7±0.5	60±3	34±3	12.7±0.9	---
75, male	6.0±0.5*	61±2	37±2*	13.6±0.8*	---
female	5.6±0.3	60±1	34±2	12.8±0.9	---

* Significantly different from controls ($p<0.05$).

APPENDIX T

COMPARISON OF THE INHALATION EFFECTS
IN RATS OF LGP 1776, LGP 1845, AND HAN
FOLLOWING 5 OR 10 DAILY EXPOSURES

COMPOUND	LEVEL mg/m³	5 Days						10 Days					
		Body Wt	OBW Ratio	RBC/Hct	Hemoglob	Heinz B	Pathol	Body Wt	OBW Ratio	RBC/Hct	Hemoglob	Heinz B	Pathol
LGP 1776	600	X	X	X	X	X	-	X	X	X	X	X	X
LGP 1845		X	X	X	X	X	-	X	X	X	X	X	X
HAN		X	X	X	-	X	-	X	X	X	X	X	X
LGP 1776	300	-	X	X	X	X	-	-	X	X	X	X	-
LGP 1845		-	X	-	-	X	-	X	X	X	-	X	X
HAN		-	X	-	-	O	X	X	X	X	-	O	X
LGP 1776	75	-	X	-	-	-	-	-	X	X	-	-	-
LGP 1845		-	X	-	-	-	-	-	X	-	-	-	-
HAN		-	-	-	-	O	-	-	X	-	-	O	-

X Significant Effect ($p < 0.05$)
- No Effect
O Not Measured